



Post-pulmonary tuberculosis complications in South Africa and a potential link with pulmonary hypertension: Premise for clinical and scientific investigations

To the Editor: The magnitude of the pulmonary tuberculosis (TB) epidemic in South Africa (SA) and globally^[1] has received increased attention. Efforts have been made to explore new and improved diagnostic^[2] and treatment strategies,^[3] but the story does not end with treatment, and TB frequently results in long-term lung damage. This may include chronic airflow obstruction, reduced lung function (forced vital capacity) and destruction of the pulmonary vascular bed in cases of advanced lung disease.^[4,5] This destruction of the vascular bed is attributed to parenchymal abnormalities that lead to reduced cross-sectional area of the pulmonary vasculature.^[6]

We highlight the fact that long-term consequences of advanced destruction of the pulmonary vasculature may occur in the absence of significant parenchymal damage, and that this is another post-TB complication that remains largely unexplored. Few previous reports^[7-9] and our clinical experience suggest that there is an association between post-TB lung disease and pulmonary hypertension (PHT). Although a proportion of patients with current TB do present with PHT,^[7,8,10] the strength of this association remains largely undefined.^[9,10] In addition, the prevalence of PHT among individuals who have been treated for pulmonary TB but who have minimal fibrotic parenchymal disease is also not known. We have noticed a paucity of literature listing TB as a potential cause of pulmonary vascular disease, or demonstrating an association between TB and PHT. Furthermore, the literature and PHT guideline documents rarely mention TB among the list of causes of group 3 PHT.^[11]

We therefore propose that a discordance may exist between our clinical reality and the literature on post-TB pulmonary vascular disease and PHT. This discordance is difficult to explain, and may in part be due to a low TB incidence in countries currently researching PHT. It is possible that in their setting they do not frequently observe patients with TB progressing to advanced lung destruction, like we do here in SA. This highlights many important unanswered questions, that include: What is the strength of the association between pulmonary TB and PHT, across the spectrum of parenchymal abnormality in TB patients? Why does the degree of right heart failure correlate so poorly with the degree of radiological changes?^[8] Does the degree of right heart failure correlate with the degree of airway obstruction/restriction regardless of the degree of radiological changes? What is the time of onset of PHT in patients who were successfully treated for TB? Lastly, do other co-factors, such as smoking, drug use or HIV, have a modifying role in the development of PHT?

Considering that in SA there were an estimated 438 000 cases of tuberculosis in 2016 alone,^[1] we highlight that further clinical

investigation and research into this disease association is important. This research is essential if we are to design treatment strategies for these patients. Without sufficient data, management decisions appear to be largely informed by anecdotes. Moreover, management algorithms are usually extrapolated from those of other group 3 PHT-related diseases (e.g. chronic obstructive pulmonary disease and pulmonary fibrosis),^[11] where the mechanism of pathology is likely to be entirely different. In our clinical experience, it is clear that TB does not end with cessation of treatment, and long after the current epidemic is over we may be left with a generation of individuals still suffering long-term consequences, one of which is PHT.

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1. World Health Organization. Global Tuberculosis Report 2017. Geneva: WHO, 2017.
2. Datta S, Saunders MJ, Tovar MA, Evans CA. Improving tuberculosis diagnosis: Better tests or better healthcare? *PLoS Med* 2017;14(10):e1002406. <https://doi.org/10.1371/journal.pmed.1002406>
3. Marx FM, Yaesoubi R, Menzies NA, et al. Tuberculosis control interventions targeted to previously treated people in a high-incidence setting: A modelling study. *Lancet Glob Health* 2018;6(4):e426-e435. [https://doi.org/10.1016/S2214-109X\(18\)30022-6](https://doi.org/10.1016/S2214-109X(18)30022-6)
4. Amaral AFS, Coton S, Kato B, et al. Tuberculosis associates with both airflow obstruction and low lung function: BOLD results. *Eur Respir J* 2015;46(4):1104-1112. <https://doi.org/10.1183/13993003.02325-2014>
5. Harries AD, Ade S, Burney P, Hoa NB, Schluger NW, Castro JL. Successfully treated but not fit for purpose: Paying attention to chronic lung impairment after TB treatment. *Int J Tuberc Lung Dis* 2016;20(8):1010-1014. <https://doi.org/10.5588/ijtld.16.0277>
6. Verma AK. Tuberculosis and pulmonary hypertension: Commentary. *Lung India*. 2016;33(2):232-233. <https://doi.org/10.4103/0970-2113.177455>
7. Ahmed AE, Ibrahim AS, Elshafie SM. Pulmonary hypertension in patients with treated pulmonary tuberculosis: Analysis of 14 consecutive cases. *Clin Med Insights Circ Respir Pulm Med* 2011;5:1-5. <https://doi.org/10.4137/CCRP.M56437>
8. Bhattacharyya P, Saha D, Bhattacharjee PD, Das SK, Bhattacharyya PP, Dey R. Tuberculosis associated pulmonary hypertension: The revelation of a clinical observation. *Lung India* 2016;33(2):135-139. <https://doi.org/10.4103/0970-2113.177433>
9. Thienemann F, Dzudie A, Mocumbi AO, et al. The causes, treatment, and outcome of pulmonary hypertension in Africa: Insights from the Pan African Pulmonary Hypertension Cohort (PAPUCO) Registry. *Int J Cardiol* 2016;221:205-211. <https://doi.org/10.1016/j.ijcard.2016.06.242>
10. Ivanov AK. [Echocardiographic evaluation of pulmonary tuberculosis in adolescent and young patients]. *Probl Tuberc* 1995;(5):32-34.
11. Galie N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Respir J* 2015;46(4):903-975. <https://doi.org/10.1183/13993003.01032-2015>

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